IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

In re: AVANDIA MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION	:	AVANDIA MDL 1871 2007-MD-1871 HON. CYNTHIA M. RUFE
THIS DOCUMENT RELATES TO: ALL ACTIONS	:	

ORDER

AND NOW, this ____ day of _____, 2010, upon consideration of Plaintiff Steering Committee's Motion to Bar Testimony as to Certain Opinions By Defendants' Expert Witnesses and Defendant GlaxoSmithKline LLC's Opposition thereto, it is hereby ORDERED that said Motion is DENIED.

BY THE COURT:

_____
Cynthia M. Rufe, J.

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE: AVANDIA MARKETING, SALES PRACTICES AND PRODUCT LIABILITY LITIGATION	: CIVIL ACTION NO. : MDL No. 1871 : 2:07-md-0 1871 -CMR
THIS DOCUMENT RELATES TO: ALL ACTIONS	

MEMORANDUM IN SUPPORT OF DEFENDANT GLAXOSMITHKLINE'S OPPOSITION TO PLAINTIFF STEERING COMMITTEE'S MOTION TO BAR TESTIMONY AS TO CERTAIN OPINIONS BY DEFENDANT'S EXPERT WITNESSES

TABLE OF CONTENTS

Page

I. INTRODUCTION 1

II. ARGUMENT 2

A. Plaintiffs Misconstrue Dr. Mayer-Davis's Proffered Testimony and Opinion. 2

B. Plaintiffs Misconstrue the Testimony Of Dr. Gavin 3

C. Plaintiffs' Challenge To Limited Portions of Dr. Gotto's Testimony Is Factually Inaccurate and Legally Unsupported. 5

1. The ACCORD patient-level data. 5

2. Calculations regarding potential statin confounding in atherosclerosis studies. 7

D. Plaintiffs' Claims About the "Unreliability" Of the Data In the Tertile Analyses Are Belied By Plaintiffs' Own Experts' Reliance On These Analyses And Go To the Weight, Not Admissibility, Of This Evidence. 9

III. CONCLUSION. 12

I. INTRODUCTION

Defendant GlaxoSmithKline LLC ("GSK") submits this opposition to Plaintiffs' Steering Committee's Motion and Memorandum of Law in Support of Motion to Bar Testimony as to Certain Opinions by Defendant's Expert Witnesses (Plaintiffs' Memo), filed on August 9, 2010 (Docket No. 746).

Plaintiffs' motion should be denied.[1] First, it seeks to exclude opinions that were never expressed by the GSK witnesses.

Second, the motion seeks to exclude reliance by GSK's experts on data that plaintiffs' experts rely on. Even if plaintiffs' contentions had any merit, the admissibility of specific items of evidence would be better addressed at trial.

GSK notes that it is not GSK's burden to establish either that Avandia is *not* "linked to the occurrence of adverse cardiovascular events,"[2] or that Avandia does *not* cause myocarial infarction – *i.e.* heart attack.[3] Rather, GSK need demonstrate only that the opinions expressed by Plaintiffs' experts and the methodology employed to reach those opinions, are scientifically unreliable and thus inadmissible.

---

[1] Plaintiffs' motion is directed at certain opinions of Drs. Mayer-Davis, Gavin and Gotto. Nothing in the plaintiffs' motion challenges the qualifications or expertise of other defense experts to opine on the same issues. Thus, plaintiffs' motion is clearly limited to the specific experts to which the motion is directed, and in no way purports to limit the opinions of other defense experts.

[2] Plaintiffs' Memo at 1.

[3] *See, e.g., Soldo v. Sandoz Pharms. Corp.*, 244 F. Supp. 2d 434, 573, 534 (W.D. Pa. 2003) ("criticisms of the epidemiologic studies upon which [defendant] relies cannot substitute for positive evidence upon which plaintiff can rely"; "It is not a defendant's burden to disprove causation"); *Wicker v. Ford Motor Co.*, 393 F. Supp. 2d 1229, 1237-1238 (W.D. Okla. 2005) (". . . it is not defendants' burden to disprove plaintiff's theory, but only to show that there is an absence of proof to support plaintiff's claim"); *Siharath v. Sandoz Pharm. Corp.*, 131 F. Supp. 2d 1347, 1358 (N.D. Ga. 2001) ("It is important to recall, however, that the burden is on Plaintiffs to show that well-conducted epidemiological studies do show a statistically significant relationship between Parlodel® and seizures and stroke. It is not Defendant's burden to show the lack of such relationship.")

II. ARGUMENT

A. Plaintiffs Misconstrue Dr. Mayer-Davis's Proffered Testimony and Opinion

Dr. Elizabeth Mayer-Davis is a professor at the School of Public Health at the University of North Carolina. She is an epidemiologist and has written extensively about diabetes. Her report addresses the epidemiological studies of Avandia, including studies that showed no progression of atherosclerosis in patients on Avandia. Not surprisingly, Plaintiffs do not contest her qualifications to testify on these subjects.[4] As an epidemiologist who has devoted her professional career to the study of diabetes and its health consequences, Dr. Mayer-Davis is eminently qualified to testify regarding the interpretation of the epidemiological studies.

Plaintiffs, however, ask the Court to exclude any testimony on a subject that she never addressed: the "pathophysiological progression of atherosclerosis as a result of exposure to [Avandia]."[5] Nowhere in either her expert reports or in her deposition testimony does Dr. Mayer-Davis offer an opinion regarding the pathophysiological *mechanism* of atherosclerotic plaque development or rupture; and nowhere does Plaintiffs' Memo identify any portion of her reports, or any deposition testimony where she purportedly offered the opinion that plaintiffs ask the Court to exclude.

Contrary to plaintiffs' suggestion, Dr. Mayer-Davis has not offered an opinion about the mechanism by which Avandia might cause heart attack.[6] Rather, the opinion that Dr. Mayer-Davis proffers is that the *epidemiological* data do not support the conclusion that

---

[4] Plaintiffs' Memo at 5.

[5] *Id.* at 7.

[6] *Id.* at 5.

exposure to Avandia worsens atherosclerosis in diabetic patients.[7] She does not address the biological, biomechanical, pathophysiological, or other mechanisms involved in the progression of atherosclerosis or the occurrence of MI. Rather, Dr. Mayer-Davis points out that in the absence of sufficient, reliable, scientific evidence to support the conclusion that Avandia is even associated with heart attack, it is premature to speculate regarding a potential causal mechanism.[8] Plaintiffs' motion as it relates to Dr. Mayer-Davis should be denied.

B. Plaintiffs Misconstrue the Testimony Of Dr. Gavin

Dr. Gavin is an eminent endocrinologist and diabetes specialist, and former President of the American Diabetes Association. He has been practicing diabetes medicine for 40 years. GSK offers Dr. Gavin's testimony on general causation, and on the absence of any connection between Avandia and Mr. Burford's death of cardiovascular causes. Plaintiffs take no issue with Dr. Gavin's ability to speak to these subjects. Rather, plaintiffs ask the Court to exclude testimony by Dr. Gavin on the exact cardiovascular cause of Mr. Burford's death – a subject on which Dr. Gavin has not offered an opinion. Whether Mr. Burford had a heart attack is a disputed issue, but not one that Dr. Gavin addressed. His report proceeds from the fact that Mr. Burford died of cardiovascular causes, without specifying the exact sequence of events

---

[7] Generic Expert Report of Elizabeth J. Mayer-Davis, Ph.D., Mar. 23, 2010 ("Mayer-Davis Report") at 28 ("there is no evidence that treatment with RSG [rosiglitazone – Avandia] progresses atherosclerosis") (Ex. 32 to GSK's Overview Memorandum on *Daubert* Issues Relating to General Causation, filed Aug. 9, 2010, Docket No. 732 ("GSK's Overview Memo")).

[8] *Id.* ("to assert a biological mechanism without confirmation of an association between RSG [rosiglitazone – Avandia] and MI is premature").

leading to Mr. Burford's death.[9] At his deposition, Dr. Gavin agreed that Mr. Burford "died a cardiovascular death and had diffuse atherosclerotic disease."[10]

Plaintiffs' Memo fails to identify any part of Dr. Gavin's report that voices an opinion on whether or not Mr. Burford had a heart attack. Plaintiffs merely quote two questions and answers from his deposition[11] in which plaintiffs asked him whether Mr. Burford had a heart attack, and in substance Dr. Gavin said he would not draw that conclusion from the evidence.

Dr. Gavin did not express an opinion, to a reasonable degree of medical certainty, that Mr. Burford did not experience a myocardial infarction. Dr. Gavin's testimony makes this clear:

> Q. And you dispute that it was a myocardial infarction?
>
> A. I'm not disputing anything. I'm simply saying based on what I've reviewed in this clinical record that what is clear about Mr. Burford and what everybody seems to agree with, and as do I from the review of the record, is that **he died a cardiovascular death and had diffuse atherosclerotic disease**.[12]

Whether Mr. Burford's cardiovascular disease resulted in a heart attack, or whether it resulted in sudden cardiac death, is immaterial to Dr. Gavin's opinion. Plaintiffs' motion as it relates to Dr. Gavin should be denied.[13]

---

[9] Case Specific Expert Report of James R. Gavin, III, M.D., Ph.D., Mar. 23, 2010, at 3 (Ex. A).

[10] Deposition transcript of James Gavin, III, M.D., *Burford v. SmithKline Beecham Corp.*, Case No. 2:07-cv-05350, June 22, 2010 ("Gavin Dep. Tr.") at 34 (Ex. B).

[11] Plaintiffs' Memo at 7-8.

[12] Gavin Dep. Tr. at 34 (emphasis added).

[13] Plaintiffs also argue that because Dr. Gavin is not a pathologist and has not examined Mr. Burford's pathology specimens he should be precluded from testifying as to Mr. Burford's cause of death. As the Fifth Circuit has recognized, however, examination of pathology specimens by a pathologist is not the only reliable way to determine cause of death. *Carrol v Morgan*, 17 F.3d 787, 790 (5th Cir. 1994)("the plaintiff argues that Dr. Bennett was not qualified to testify as to Carroll's cause of death because Dr. Bennett is not a pathologist. *Daubert* does not support plaintiff's position that the subject of Carroll's death falls within the exclusive confines of pathology").

C. Plaintiffs' Challenge To Limited Portions of Dr. Gotto's Testimony Is Factually Inaccurate and Legally Unsupported

Dr. Gotto is a professor and dean of Cornell Medical College and a specialist in cardiovascular disease. Dr. Gotto has served on innumerable committees and boards, including being the Chairman of the Data Safety Monitoring Board ("DSMB") for the ACCORD trial, which was sponsored by the National Heart, Lung and Blood Institute. Dr. Gotto has been principal investigator in a number of clinical trials involving the treatment of atherosclerosis. Throughout his professional career, his research has focused on lipid research and the causes and treatment of atherosclerosis. Dr. Gotto has served as the President of the American Heart Association and the International Atherosclerosis Society.

Plaintiffs present a *Daubert* challenge arguing that, because Dr. Gotto "considered" the patient-level data from the ACCORD study, and because plaintiffs do not have access to it, he should be "precluded from offering any opinions based on such data."[14] Plaintiffs offer no evidence, however, that either GSK or Dr. Gotto has the patient-level data from that study. Plaintiffs also allege that Dr. Gotto undertook certain calculations relating to statin use in other studies, which he did not present in his expert report, and therefore Dr. Gotto must be "barred" from discussing these calculations.[15] Neither of these challenges is factually accurate or legally supported.

1. The ACCORD patient-level data.

Long before his involvement in this litigation, Dr. Gotto served as the Chair of the DSMB of the ACCORD trial, which examined whether intensive glucose lowering therapies

---

[14] Plaintiffs' Memo at 10.

[15] *Id.*

would reduce cardiovascular risk.[16] Rosiglitazone was among the several therapies examined in this study. In February of 2008, before its completion, the DSMB ordered the study halted because of a detected increase in mortality in the group of study subjects receiving intensive glucose lowering medications. Plaintiffs contend that Dr. Gotto based his opinions on patient-level data from ACCORD.

Contrary to plaintiffs' contentions, Dr. Gotto never indicated that he relied on or considered any patient-level data from the ACCORD study for the opinions he has expressed in this case.[17] Indeed, neither Dr. Gotto's original expert report, nor his supplemental expert report, even references patient level data from the ACCORD study. At Dr. Gotto's deposition, Mr. Cartmell asked Dr. Gotto if he had "look[ed] at the patient level lipid data" from ACCORD, whether he had "knowledge about [it]," and whether he could "recall it."[18] Dr. Gotto, however, made clear that he did not base his opinions in this case on such data:

> Q. Is the ***basis for that opinion*** from looking at patient-level data or just the published publications and what they include related to lipid data?
>
> A This is ***based on*** looking at the publications.[19]

Plaintiffs' motion to preclude Dr. Gotto's testimony based on "patient-level" data from ACCORD should be denied as moot.

---

[16] The Action to Control Cardiovascular Risk in Diabetes (ACCORD) Study Group, Effects of Intensive Glucose Lowering in Type 2 Diabetes, 358 NEW ENG. J. MED. 2545 (2008) (Ex. 50 to GSK's Overview Memo).

[17] Questions at the deposition about ACCORD patient-level data only came up because counsel for the plaintiffs, Thomas Cartmell, had previously approached Dr. Gotto to serve as a plaintiffs' expert in this litigation. Dr. Gotto declined but not before he and Mr. Cartmell had a conversation about rosiglitazone, the litigation and the ACCORD study. *See* Deposition Transcript of Antonio M. Gotto, Jr., M.D., D.Phil., *In re Avandia*, MDL No. 1871, June 22, 2010 ("Gotto Dep. Tr.") at 58:7-19 (Ex. C).

[18] Gotto Dep. Tr. at 57:5-12 (Ex. C).

[19] *Id.* at 269:16-21 (emphasis added).

Although plaintiffs' motion does not seek the disclosure of patient-level data from the ACCORD study, to the extent that plaintiffs imply that such data should have been disclosed pursuant to Rule 26(a)(2)(B), there is no legal basis to support this claim. "As the plain terms of the Rule make clear . . . Rule 26(a)(2)(B) only applies to material disclosed to and considered by an expert witness **for purposes of his or her expert report and testimony – that is, information the expert receives or considers in his or her capacity as a testifying expert witness**." *Bro-Tech Corp. v. Thermax, Inc.*, 2008 WL 724627, at *2 (E.D. Pa. Mar. 17, 2008) (emphasis added); *Synthes Spine Co., L.P. v. Walden*, 232 F.R.D. 460, 464 (E.D. Pa. 2005) (stating that Rule 26(a)(2)(B) requires disclosure of information considered by the expert "in connection with the formulation of his opinions"). Since it is indisputable that Dr. Gotto did not "consider" the ACCORD patient-level data "for purposes of his expert report and testimony," there was no obligation to disclose the ACCORD patient-level data to the plaintiffs, even if Dr. Gotto had such data.

2. Calculations regarding potential statin confounding in atherosclerosis studies.

Plaintiffs allege that Dr. Gotto made complex calculations about the implications of statin use in atherosclerosis progression studies which were not described in his expert report, thereby depriving plaintiffs from being able to evaluate Dr. Gotto's methodology in this regard.[20] This is a misrepresentation of Dr. Gotto's testimony about these "calculations."

Dr. Gotto's professional career has focused on statins and their ability to reduce cardiovascular risk. Primary research into statins and their effects on cardiovascular disease has been at the center of his scientific career for the past 40 years. As his CV and his deposition

[20] Plaintiffs' Memo at 10.

testimony reveal, it is an essential part of his professional activities to review and evaluate statin data in epidemiological studies such as the atherosclerosis progression studies. It could not have been a secret to plaintiffs' counsel that when evaluating studies, such as the IVUS and CIMT studies (which are clearly cited in his expert report and which included statin use and lipid data), Dr. Gotto would bring his vast experience as a researcher and study investigator to bear as part of that evaluative process.

When he was asked at deposition whether he did any specific analysis concerning disparate statin use in any of the IVUS or CIMT studies and whether such use confounded the results of these studies,[21] Dr. Gotto responded that "where statins were used [I] tried to make an *estimate* about what the impact might be but I can't give you a complete analysis of each one of the studies."[22] Mr. Cartmell then asked: ". . . my question is not about the specific study . . . My question is: Are you able to make a complete analysis of whether there was statin confounding based on what the LDL did in each of the arms?"[23] Dr. Gotto indicated that his estimate would not be precise but would be "fairly accurate" and then proceeded to describe his method for making such an estimate.[24] This "calculation" was a matter of simple arithmetic, derived from data presented in each of the published IVUS or CIMT studies and based on Dr. Gotto's experience with the way in which statins influence LDL-C.[25] Moreover, plaintiffs' counsel had ample opportunity to question Dr. Gotto about this calculation.

---

[21] Gotto Dep. Tr. at 318:6-10 (Ex. C).

[22] *Id.* at 319:17-23 (emphasis added).

[23] *Id.* at 321:21-322:1.

[24] *Id.* at 322:5-15; 322:25-323:18.

[25] *Id.*

Federal courts interpreting Rule 26(a)(2)(B) have emphasized that "neither the plain language of the rule nor its purpose compels disclosure of every calculation or test conducted by the expert during formation of the report." *See e.g.*, *Flebotte v. Dow Jones & Co., Inc.*, 2000 WL 35539238, at *7 (D. Mass. 2000); *Anderson v. Ridge Tool Co.*, 2008 WL 3849923, at *3 (E.D. Ky. Aug. 14, 2008) (noting that an expert "is permitted to rely on his experience to come to basic conclusions and calculations"). Indeed, "[t]o impose such a requirement would force all expert witnesses to provide the basic tenets of their fields in every case in which they testify." *Anderson*, 2008 WL 3849923 at *3. For all of these reasons, plaintiffs' argument that Dr. Gotto's "calculations" regarding the impact of statin use in CIMT/IVUS studies should be excluded is meritless.

D. Plaintiffs' Claims About the "Unreliability" Of the Data In the Tertile Analyses Are Belied By Plaintiffs' Own Experts' Reliance On These Analyses And Go To the Weight, Not Admissibility, Of This Evidence

Plaintiffs assert that unidentified GSK experts rely on certain "tertile charts" (which plaintiffs did not submit as exhibits) and that the charts are "misleading."[26] Plaintiffs do not ask the Court to preclude any GSK expert from testifying to any opinion on the subjects the charts address, but rather ask the Court to bar any GSK expert (but not any plaintiffs' expert) from relying on the charts. Plaintiffs offer no support for making such a request under *Daubert*, and, even if the request had any merit, it would be appropriate only for a motion *in limine*. Plaintiffs' request should be denied.

In 2007, GSK evaluated whether any correlation existed between LDL changes experienced by patients taking Avandia and the occurrence of myocardial infarction. To examine this question, GSK looked at patients who experienced myocardial infarction and

[26] Plaintiffs' Memo at 10-11.

divided those patients into three groups ("tertiles") based on changes in LDL cholesterol. No correlation was observed, and GSK concluded that "it is unlikely that the early change in LDL-c is associated with myocardial infarction."[27] These "tertile analyses" were presented to the FDA Advisory Committee members in 2007, and plaintiffs have had copies since that time.

Plaintiffs argue that the tertile analyses have missing values and are therefore confusing, "simply not reliable," and "cannot properly inform a scientific opinion."[28] What plaintiffs fail to tell the Court is that their own expert – Dr. Swirsky – has testified that the tertile analyses merit weight and inform his opinion, notwithstanding the "missing data points":

> Q. Is it your testimony that there's a statistically significant difference between the tertiles?
>
> A. No, we can't talk about statistical significance here, but it's in keeping with all of the other data, and you – and you know we can't talk about statistical P values and significance here because of the numbers. They're – they're small. And that there's a lot of missing data points.
>
> Q. So you don't put any weight on the tertile analysis based on its deficiencies?
>
> A. No, I do put weight on it. That it's not – it didn't show me data counter to what I believe to be the truth and logic. And it – it's reassuring that the expected data – in my mind, the expected data is the observed data. Granted we're missing data points. But – but the expectation and the observation lineup is congruent.[29]

In fact, Dr. Swirsky explained the reasons for his failure to analyze whether patients with LDL increases had increases in adverse cardiovascular outcomes as follows: "I

---

[27] GlaxoSmithKline's Advisory Committee Briefing Document, prepared for the Endocrinologic and Metabolic Drugs Advisory Committee; Drug Safety and Risk Management Advisory Committee Meeting on July 30, 2007 at 79 (Ex. D).

[28] Plaintiffs' Memo at 11.

[29] Deposition transcript of Brian C. Swirsky, M.D., *In re Avandia*, MDL No. 1871, Apr. 23, 2010 ("Swirsky Dep. Tr.") at 185-86 (Ex. 47 to GSK's Overview Memo).

didn't feel I needed to do that. There was already an analysis that looked at LDL Tertile increases and cardiovascular event rate trends so I – I felt that that data already existed and looked like a trend that the higher the LDL cholesterol, the more event rates."[30] The fact that plaintiffs' own expert relied on these same analyses for his opinions is, in and of itself, reason to reject plaintiffs' arguments. *Lithuanian Commerce Corp., Ltd. v. Sara Lee Hosiery*, 202 F. Supp. 2d 371, 377 (D.N.J. 2002) (rejecting as "unpersuasive" plaintiff's claim that the data underlying the defense expert's opinion were unreliable where plaintiff's own expert relied on the same data).

Even if plaintiffs' arguments had any merit, they clearly go to the weight to be given to the tertile analyses, and not to the admissibility of this evidence.[31] Thus, plaintiffs' arguments regarding alleged inadequacies of the tertile analyses are fodder for cross examination and not a basis for exclusion.

---

[30] *Id.* at 182. Another plaintiffs' expert, Dr. Brinton also referred to the tertile analysis when asked whether he has "done anything to correlate heart attacks in patients taking Avandia with changes in LDL." Dr. Brinton responded as follows: "[t]he one thing that I have done is to look at a tertile analysis from the ICT in which there was an analysis done by GSK looking at the change in LDL cholesterol by tertiles and then the risk of cardiovascular event. So I've looked at that, and that's one analysis I've done." Deposition transcript of Eliot A. Brinton, M.D., *In re Avandia*, MDL No. 1871, Apr. 28, 2010 ("Brinton Dep. Tr.") at 332 (Ex. 37 to GSK's Overview Memo).

[31] *Hemmings v. Tidyman's Inc.*, 285 F.3d 1174, 1188 (9th Cir. 2002)("in most cases, objections to the inadequacies of a study are more appropriately considered an objection going to the weight of the evidence rather than its admissibility. . . . Vigorous cross-examination of a study's inadequacies allows the jury to appropriately weigh the alleged defects and reduces the possibility of prejudice").

III. CONCLUSION.

For the reasons stated above, plaintiffs' motion should be denied in its entirety.

Date: August 30, 2010

Respectfully submitted,

/s/ Nina M. Gussack
Nina M. Gussack (Pa. Bar No. 31054)
Anthony C.H. Vale (Pa. Bar No. 28139)
PEPPER HAMILTON LLP
3000 Two Logan Square
18th & Arch Streets
Philadelphia, PA 19103
(215) 981-4000

Tamar P. Halpern
Cindy Kaplan Bennes
PHILLIPS LYTLE LLP
340 HSBC Center
Buffalo, NY 14203
(716) 847-8400

Attorneys for Defendant GlaxoSmithKline LLC (f.k.a. SmithKline Beecham Corporation d/b/a GlaxoSmithKline)

CERTIFICATE OF SERVICE

I hereby certify that on August 30, 2010, I caused a true and correct copy of the foregoing Memorandum in Support of Defendant GlaxoSmithKline's Opposition to Plaintiff Steering Committee's Motion to Bar Testimony As to Certain Opinions By Defendant's Expert Witnesses to be served by electronic mail and Federal Express upon plaintiff's counsel as follows:

Joseph J. Zonies, Esq. (via PDF and Federal Express)
Reilly Pozner LLP
The Kittredge Building
511 Sixteenth Street, Suite 700
Denver, Colorado 80202
jzonies@rplaw.com

Thomas P. Cartmell, Esq. (via PDF and Federal Express)
Wagstaff & Cartmell LLP
4740 Grand Ave., Suite 300
Kansas City, MO 64112
tcartmell@wcllp.com

Thomas Mellon, Esq. (via PDF and Federal Express)
Mellon Webster & Shelly, PC
87 North Broad Street
Doylestown, PA 18901
TMellon@MellonWebster.com

/s/ Jessica A. Rickabaugh
Jessica A. Rickabaugh

Date: August 30, 2010